Use of repellents by travellers: A randomised, quantitative analysis of applied dosage and an evaluation of knowledge, Attitudes and Practices (KAP)

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Use of repellents by travellers: A randomised, quantitative analysis of applied dosage and an evaluation of knowledge, Attitudes and Practices (KAP)

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ABSTRACT

Background: Prevention of arthropod-borne infections hinges on bite prevention. We aimed to investigate travellers' use of repellents.
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Results: Some 200 volunteers travelling to mosquito borne infection endemic areas were recruited. The mean concentration of active substance achieved on the skin of the left arm was 0.52 mg/cm^2 of DEET/Icaridin spray versus 0.21 mg/cm^2 of Icaridin lotion. These levels are below the recommended protective dose (1 mg/cm^2) for each formulation. Women were significantly more likely to apply a higher, protective dose of repellent. Travellers to Africa, women and older participants showed higher projected adherence to AVPM.
Conclusions: Only 2.5% of recruited travellers applied the recommended protective dose of repellent. Women and older travellers are the most adherent users of repellents. The pre-travel health consultation should provide more information on the application quantity and correct use of repellents.

1. Background

Mosquito borne infections such as malaria, dengue, chikungunya, Zika and Japanese encephalitis have an expanding geographic range worldwide. They constitute an important global burden of disease with significant mortality, morbidity and long-term illness sequelae that affect hundreds of millions of people living in endemic areas [1]. Travellers visiting affected areas are challenged as there are few traveller vaccines available, with the exception of Japanese encephalitis, and most protective approaches rely on the prevention of mosquito and arthropod bites [2].

Use of repellents is a key measure in the prevention of mosquito bites. A repellent is defined as a "chemical volatile substance that induces arthropods to move in the opposite direction from its source" [3]. Repellents are volatile, usually oily substances whose odour prevents the landing of mosquitoes and other arthropods on the skin. An ideal repellent should protect against a wide variety of arthropods for several hours and withstand removal when sweating, rubbing or washing without causing adverse events nor damage clothes or accessories (e.g. bracelets, watches, eyeglass frames) [3,4]. Mosquitoes are still attracted by humans after repellent application, however the mosquitoes are repelled when coming close because of the volatile ingredients of the repellent. This protective air layer extends only for a few centimetres, therefore the repellent has to be applied all-over the exposed skin [5,6].

N,N-Diethyl-3-methylbenzamide (DEET, formerly N,N-Diethyl-m-toluamide), developed by the United States Department of Agriculture and on the market since 1957, is considered to be the most effective and widely used repellent worldwide [7]. It is also used as the standard reference repellent of the WHO [8,9]. DEET is a synthetic, oily and volatile liquid, insoluble in water, but very soluble in alcohol. The repelling effect of DEET is a result of its affinity and binding to odorant receptors as well as to chemoreceptors of the mosquitoes [10]. The efficacy of repellents containing DEET has been shown in both laboratory conditions and field studies not only against mosquitoes, but

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also against many other blood-feeding arthropods such as black flies, ticks and leeches [6,11]. The most frequently observed adverse events associated with DEET are mild skin irritations. There have been some reports of encephalopathy after DEET exposure, notably in children after ingestion, but also after dermal exposure [12]. However, the causal role of DEET in these cases is debatable and taking into account the extensive use of DEET worldwide (approximately 200 million applications per year), the number of reported adverse events is low [13–15]. Risk assessments by the US Environmental Protection Agency (EPA) as well as a clinical trial found no connection between encephalopathy and use of DEET, and no toxic risk or severe effects except after inappropriate use (ingestion, direct inhalation, or eye exposure) [15]. After dermal application, low levels of DEET and its metabolites were detected in blood plasma. However, less than 9% of the amount applied was absorbed [16]. DEET can also cross the placenta, but a small study of DEET exposure (1.7g/day) in second and third trimester pregnancies in Thailand did not detect adverse effects in either exposed women or infants [17]. DEET is considered to be safe from second trimester onwards, while breast-feeding and for children aged over 8 weeks [18], but recommendations regarding the use of DEET for children vary by country. Furthermore, there are no published data on the use and tolerability of DEET by pregnant women in the first trimester. In general for travellers, formulations with concentrations of 20% DEET and higher are considered to provide good and long lasting protection [19].

Icaridin (also known as Picaridin, Bayrepel, KBR3023) is a synthetic, volatile, and water-insoluble oily repellent. It is almost as effective as DEET and shows a lower rate of adverse events [20]. Adverse events reported to the National Poison Data System included ocular irritation, reddened eyes, vomiting, and oral irritation. Symptoms were usually mild and no serious adverse events (life threatening, hospitalization required, or persistent disability) or cases of death were reported [21]. Formulations on the market usually contain from 5% up to 30% Icaridin, while a higher concentration provides a longer lasting protection [6]. Icaridin is supposed to bind to the same or similar olfactory receptors and chemoreceptors as DEET [22].

To provide a good protection, repellents should be applied in a sufficient amount on the skin. Rutledge and Colleagues developed a mathematical model to describe the persistence and effectiveness of repellents on the skin over 30 years ago [23]. The duration of the protection rises with the applied dose of active ingredient and reaches a plateau at a skin concentration of 2 mg/cm^2. A dose above 1 mg/cm^2 is considered to provide a reasonable and long lasting protection i.e. several hours under laboratory conditions [24]. In studies evaluating lower doses of active ingredients, protection levels were sufficient in the first hour after application, but then decreased slowly [6,25]. The WHO guidelines for efficacy testing recommend a dose of 1 ml of product for 600 cm^2 (approximately 1.67 mg/cm^2) without considering the concentration of active ingredient [8]. This reference dose is used by default in laboratories evaluating repellents. The American guidelines from the EPA do not recommend a standard dose for application. The products are applied *ad libitum* and the mean dose is measured [26].

A study from the UK with 74 participants living in the UK and 54 travellers to Kenya and India showed that repellent users rarely achieved the required protective concentration of 1 mg/cm^2 DEET. On the neck and on the arms the achieved skin concentration was below the required concentration [27]. Another study from the UK showed that the amount applied was greater when participants used a lotion compared to using a spray. However, the number of participants in that evaluation was very small (n = 12) and the results may not be representative [28].

A major issue for travellers is the adherence with repellents and other anti-vectorial protective measures (AVPM). A study among United States Community Service Volunteers returning from the Dominican Republic showed rather good adherence to AVPM. More than 90% used repellents and a bed net [29]. However, another American study with the Department of Defence beneficiaries travelling to regions for vector borne diseases showed a rather poor overall compliance with AVPM. 53% used skin repellents, 16% used permethrin on clothing and 39% used a bed net [30]. Similar or even poorer compliance rates have been shown in other studies with civil travellers [31,32]. The recommendations for the quantitative use of repellents provided by the manufacturers on the product packaging are very limited and therefore may not contribute to appropriate application doses and rates.

The aim of this study was to measure, quantitatively, the amount of repellent applied to the arm with two different application forms (spray, lotion) as well as to evaluate the knowledge, attitude and practice of traveller, with regard to bite protection and their intended AVM approaches when visiting regions endemic for mosquito borne infections.

2. Methods

2.1. Study design

This study was carried out from April until June 2018 with 200 subjects (99 male and 101 female subjects) recruited from clients attending the Centre for Travel Medicine of the University of Zurich, WHO Collaborating Centre for Travellers' Health, who were going to regions endemic for mosquito borne infections. The study participants were informed about the study in order of arrival at the travel clinic while they waited for their pre-travel consultation in the waiting room. All persons who gave informed consent (approximately 50% of those asked) were included into the study. The exact response rate was not recorded. The recruitment was stratified in order to obtain equal numbers of males and females for the study and within repellent groups. Two repellents, a spray containing 30% DEET and 20% Icaridin (Nobite® extreme) and a lotion containing 20% Icaridin (not yet marketed), were compared with regard to the applied dose, tolerability, and usability of the products. The repellents were provided in neutral containers without brand names. The subjects were randomised into two equally sized and gender balanced groups each applying one of the repellents. They were asked to apply the repellent on their left arm without any further instructions. The dose applied was estimated by measuring the loss of weight of the repellent container and the concentration of the active ingredient on the skin was calculated according to the formula described by Goodyer and Patel (Fig. 1) [28].

After the application of the repellents, the subjects were asked to complete a questionnaire about the tolerability and usability of the applied repellents and about their knowledge, attitude, and practice (KAP) of AVPM in general. Yes-no questions were used to evaluate adverse events of the repellents. To rate the user acceptability and the odour of the repellents, visual analogue scales were used. To evaluate the KAP, the subjects could choose from given answers. The subjects were recruited before receiving pre-travel health advice at the travel clinic.

2.2. Sample size considerations

The sample size calculation used the amount of repellent applied as primary outcome. Data for sample size calculation was taken from the study by Thrower and Goodyer [27]. The sample size calculation based on a between-group difference in the primary outcome of 0.12 mg/cm^2, an anticipated standard deviation of 0.29, a significance level of 5% and power of 80%. This sample size calculation resulted in 75 persons per group, the group size was increased to 100 persons per group to ensure equal numbers of both sexes.

2.3. Statistical analysis

The software Stata (Version 13.1) was used for the data analysis.

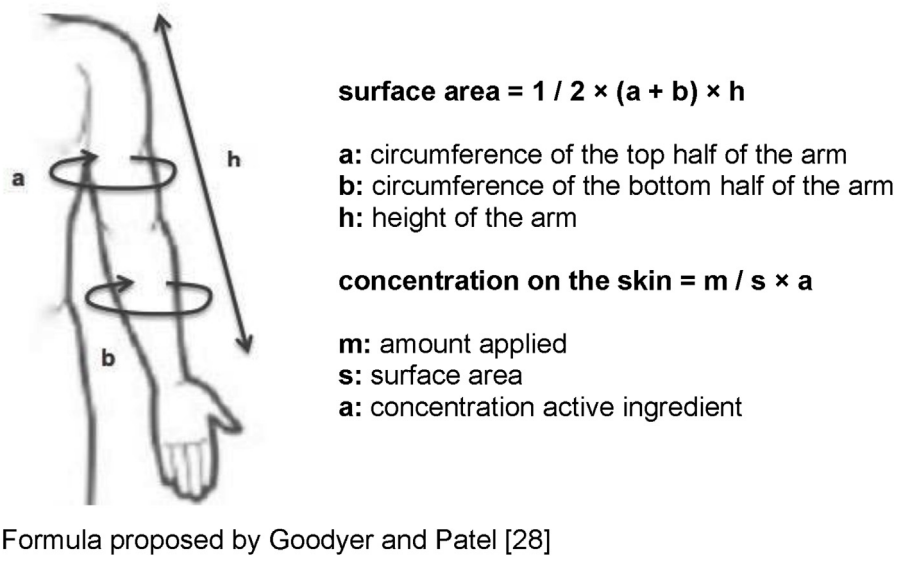

Fig. 1. Calculation of the amount of repellent applied on the left arm*.
* Formula proposed by Goodyer and Patel [28].

Descriptive statistics included mean and standard deviation for the continuous variables, as well as counts and percentage of total for the categorical variables. Ordinally scaled variables were displayed as median and interquartile range. T-test and ANOVA were used to compare the amount of repellents applied across randomized groups. Fisher's exact tests or chi square tests were performed for the analysis of the KAP questionnaire. The p-values for adverse events and KAP questionnaire were considered exploratory. Other p-values < 0.05 were considered as statistically significant.

2.4. Ethical considerations

The protocol synopsis of this study was reviewed by the Cantonal Ethics Committee of Zurich (BASEC Request-Nr. Req-2018-00139). The project did not fall within the scope of the Human Research Act (HRA) since repellents are classified as cosmetic products in Switzerland. Therefore, no formal ethics committee approval was required. Each participant signed an informed consent form at the beginning of the study after a thorough explanation of the study's procedures and objectives.

3. Results

3.1. Study population

In total, 200 subjects, 99 male and 101 female persons, were recruited prior to receiving pre-travel advice and included in this study. The mean age was 35 years. The range was from 18 to 70 years. With regard to the age distribution, 89 (44.5%) of the participants were younger than 30 years, 54 (27%) were aged between 30 and 40 years, and 57 (28.5%) were 40 years or older. Slightly less than half of the participants 99 (49.5%) were male. South America and South East Asia were the most popular travel destinations with 64 (32%) respectively 63 (31.5%) travellers. 28 (14%) travellers were going to East Africa and 13 (6.5%) to West Africa, the high-risk malaria regions. For 170 (85%) subjects, the main purpose of their trip was leisure/tourism, 16 (8%) were visiting friends and relatives (VFR), 14 (7%) were going on a business trip. 136 (68%) had previously visited countries endemic for mosquito borne infections (Table 1).

3.2. Repellents

Only 5 subjects (2.5%), solely in the group using the formulation of DEET plus Icaridin, achieved the protective levels of 1 mg/cm^2 active ingredient proposed by Buescher and Rutledge [24]. The mean dose of repellent applied on the left arm was 1.04 mg/cm^2 of DEET/Icaridin spray (corresponding to active substance concentration of 0.52 mg/cm^2) versus 1.07 mg/cm^2 of Icaridin lotion (active substance concentration of 0.21 mg/cm^2) (Table 2). Hence, the subjects did not apply more of the repellent when using a lotion compared to a spray ($p = 0.389$).

In general, women applied a higher dose compared to men. In the DEET/Icaridin spray group, women applied 0.37 mg/cm^2 more than men ($p = 0.020$). In the Icaridin lotion group, the difference was 0.14 mg/cm^2 ($p = 0.138$) (Table 2).

Regarding the active ingredients, subjects using the DEET/icaridin spray (50% active ingredients) reached a mean concentration of 0.52 mg/cm^2, whereas subjects using the icaridin lotion (20% active ingredient) reached only 0.21 mg/cm^2 ($p = < 0.001$) (Figs. 2 and 3).

Regarding the age, subjects were grouped into three categories (18–29, 30–39, and 40 + years). In the age group 40+, the applied dose was highest (1.36 mg/cm^2 DEET/Icaridin spray; 1.22 mg/cm^2 Icaridin lotion), followed by the youngest group 18–29 (1.0 mg/cm^2 DEET/Icaridin spray; 0.95 mg/cm^2 Icaridin lotion). The group aged 30–39 years applied the lowest doses (0.8 mg/cm^2 DEET/Icaridin spray; 1.11 mg/cm^2 Icaridin lotion). However, the differences between the age groups were not significant (DEET/Icaridin spray group: $p = 0.069$, Icaridin lotion group: $p = 0.192$) (Table 2).

No serious adverse events were reported. Six subjects in the DEET/Icaridin spray group and six in the Icaridin lotion group had a burning sensation on the skin after the application. One participant in the DEET/Icaridin spray group had a reddening of the skin compared to three in the Icaridin lotion group ($p = 0.621$). Four subjects, only in the DEET/Icaridin spray group, felt a burning sensation in the airways ($p = 0.121$). 48 participants in the DEET/Icaridin spray group described a sticky feeling on the skin and 41 in the Icaridin lotion group ($p = 0.319$) following application of the repellent (Table 3).

There was no difference between the two repellents with regard to the odour, both reached mean marks of 3.09 out of 5 (1 = unpleasant, 5 = pleasant) on the visual analog scale. The usability of the DEET/Icaridin spray was slightly better rated with 1.35 (1 = easy to use, 5 = complicated to use) compared to the Icaridin lotion with 1.52

Table 1
Number of travellers intending to travel to different travel destinations, sex, mean age, the purpose of their trip, and the number of travellers with previous travel experience to countries endemic for mosquito borne infections.

Destination	Number of Travellers	Male	Mean Age	Purpose of the trip			Previous Trips[a]
				Tourism	Business Trip	VFR	
South America	64	33 (51.5%)	35.9	50 (78.1%)	5 (7.8%)	9 (14.1%)	47 (73.4%)
South East Asia	63	33 (52.4%)	28.7	58 (92.1%)	3 (4.8%)	2 (3.2%)	35 (55.6%)
East Africa	28	14 (50.0%)	35.6	26 (92.9%)	2 (7.1%)	0	20 (71.4%)
Southern Africa	16	6 (37.5%)	45.1	16 (100%)	0	0	14 (87.5%)
West Africa	13	5 (38.5%)	33.9	6 (46.2%)	3 (23.1%)	4 (30.8%)	9 (69.2%)
Central America	12	7 (58.3%)	40.5	11 (91.7%)	1 (8.3%)	0	7 (58.3%)
Middle East	3	1 (33.3%)	41	2 (66.7%)	0	1 (33.3%)	3 (100%)
Australia	1	0	18	1 (100%)	0	0	1 (100%)
Total	200	99 (49.5%)	34.5	170 (85.0%)	14 (7.0%)	16 (8.0%)	136 (68.0%)

[a] Travellers who had previously visited countries endemic for mosquito borne infections.

Table 2
Mean dose of repellent applied [mg/cm^2] (SD).

	DEET/Icaridin spray	P-value	Icaridin lotion	P-value
Total	1.04 (0.91)		1.07 (0.65)	0.389
Male	0.84 (0.55)	0.020*	1.00 (0.54)	0.138
Female	1.21 (1.11)		1.15 (0.76)	
Age 18–29 years	1.00 (0.99)	0.069	0.95 (0.65)	0.192
Age 30–39 years	0.79 (0.28)		1.11 (0.52)	
Age 40+	1.36 (1.12)		1.22 (0.74)	

*p-values < 0.05 are considered significant.

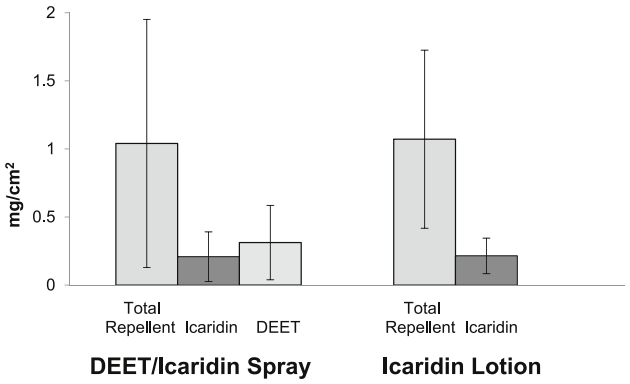

Fig. 2. Applied doses of repellents and their active ingredients on the left arm.

(Table 3).

3.3. Knowledge, attitude, and practice

Six men (6%) stated that they would never use repellents on their trip. 45 subjects (22.6%) intended to use them once per day, 95 (47.7%) twice per day, 41 (20.6%) every 5 h and 12 (6%) every 3 h. In general, women intended to use the repellents more often per day than men (Table 4). Most of the participants (126, 63%) intended to use the repellents during day- and night-time, 41 (20.5%) only during night-time and 27 (13.5%) only during daytime. 154 (77%) planned to use further measures against mosquito bites, among which the most mentioned were long sleeved clothes (55%) and mosquito nets (46%). 88 (87.1%) women intended to use further measures, compared to 66 (66.7%) men (p = 0.001) (Table 5).

Regarding the travel destinations and the intended use of additional anti-vectorial prevention measures, travellers to East Africa, West Africa, and Southern Africa stated the highest projected adherence rates. Travellers to South America and South East Asia showed lower projected adherence rates, travellers to Central America and Middle East had the lowest projected adherence rates (Table 6).

The subjects in the oldest age group (40 + years old) showed the highest projected adherence rates with regard to the use of additional mosquito bites prevention measures (49; 86%), followed by group 30–39 (43; 79.6%) (p = 0.064). The youngest group showed the poorest projected rates (62; 69.7%). Tourists and subjects visiting friends and relatives stated similar projected adherence rates (129; 75.9% respectively 12; 75%). Business travellers had a higher projected adherence rate (13; 92.9%). Travellers who had been to endemic countries before showed slightly higher projected adherence rates (107; 78.7%) than inexperienced travellers (47; 73.4%), (p = 0.411).

4. Discussion

Malaria and arboviral infection prevention strategies pose major challenges in travel medicine [33–35] and repellents play a key role in prevention. This study was a quantitative approach to provide a better understanding of the adherence to repellents by travellers and of their knowledge, attitude, and practice to AVPM in general. Most travellers in our study intended to use repellents on their trip, however the doses applied were often too low to provide sufficient protection levels. Travellers to Africa, women and people aged over 40 showed the best compliance to AVPM.

Looking at the amount of repellent applied, two variables have to be considered, the total amount of repellent applied and the concentration of active substance attained on the skin. The total amount of repellent was used to compare the formulation of the repellents, in this study a spray versus a lotion. The difference in quantity applied between the two repellents was small (0.032 mg/cm^2) and statistically not significant (p = 0.389). Accordingly, the formulation (i.e. spray versus lotion) of the repellent does not seem to have a considerable influence on the applied dose.

The concentration of active substance reached on the skin provides the protection against mosquito bites. Subjects applying the DEET/Icaridin spray (50% active substance) reached higher average concentrations on the skin (0.52 mg/cm^2) than subjects applying the Icaridin lotion (20% active substance, 0.214 mg/cm^2). However, with both repellents the average concentration was well below 1 mg/cm^2, i.e. the recommended protective level. Our results also show a wide range and large standard deviations of doses applied, particularly in the DEET/Icaridin spray group. Only 5 subjects (5%) in the group using the DEET/Icaridin spray achieved the recommended protective level of 1 mg/cm^2 versus none of the users of the Icaridin lotion. Furthermore, a loss of repellent during the application process, especially a residue on the hands, should be considered and therefore the actual skin concentration might be even lower in some cases. Thus, it appears from our

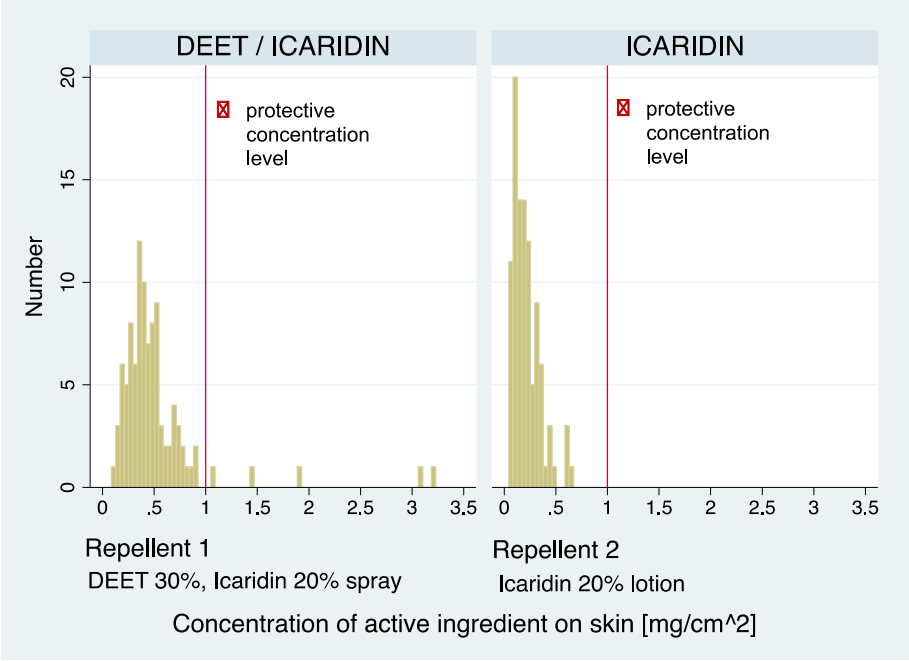

Fig. 3. Distribution of the concentration of active ingredient reached on the skin.

Table 3
Group data and adverse events of repellents.

Repellent	DEET/Icaridin spray	Icaridin lotion	P-value[a]
Number	100	100	
Mean Age (SD)	34.02 (12.49)	34.93 (13.34)	
Male	46	53	
Burning on skin	6	6	p = 1.000
Redness of skin	1	3	p = 0.621
Sticky feeling	48	41	p = 0.319
Burning in the airways	4	0	p = 0.121
Odour, median[b] (IQR)	3.09 (2)	3.09 (0)	p = 1.000
Usability, median[c] (IQR)	1.35 (1)	1.52 (1)	p = 0.098

[a] p-values are considered exploratory.
[b] Visual analog scale: 1 = unpleasant, 5 = pleasant.
[c] Visual analog scale: 1 = easy to use, 5 = complicated to use.

Table 4
How often travellers intend to apply repellents per day.

	Male (n = 98)	Female (n = 101)	Total (n = 199)
Never	6	0	6
Once per day	23	22	45
Twice per day	46	49	95
Every 5 h	19	22	41
Every 3 h	4	8	12

results that this formulation containing just 20% of active substance, i.e. 20% Icaridin, will not suffice as a repellent. Higher concentrations of Icaridin are indicated.

Subjective repellent tolerability was good and no serious adverse events were observed, as we expected from previous risk assessments and from the literature [14,15,21] which shows that topically applied repellents are generally well tolerated. With regard to cosmetic properties of the two formulations, the number of subjects reporting "a sticky feeling on the skin" after the application was only slightly lower in the Icaridin group compared to the DEET/Icaridin group and statistically not significant. This is interesting as DEET is often described to leave an oily, greasy or sticky feeling on the skin [4]. Another issue is the perceived tolerability of repellents by travellers. Some travellers might fear adverse events after using repellents, which might reduce the adherence rate. Travellers' perceived tolerability of repellents is an area for further research.

Table 5
Mosquito bite prevention measures and the number of travellers who intend to use them.

Measures	Total	Male (n = 99)	Female (n = 101)	P-value*
Any measure	154 (77.0%)	66 (66.7%)	88 (87.1%)	p = 0.001
Long sleeved clothing	119 (59.5%)	51 (51.5%)	68 (67.3%)	p = 0.023
Mosquito net	99 (49.5%)	39 (39.4%)	60 (59.4%)	p = 0.005
Light coloured clothing	39 (19.5%)	16 (16.2%)	23 (22.8%)	p = 0.238
Impregnation of clothes	39 (19.5%)	16 (16.2%)	23 (22.8%)	p = 0.238
Air conditioning	25 (12.5%)	14 (14.1%)	11 (10.9%)	p = 0.238
Perfumed candles[a]	17 (8.5%)	5 (5.1%)	12 (11.9%)	p = 0.127
Vitamin B[a]	5 (2.5%)	2 (2.0%)	3 (3.0%)	p = 1.000
Ultrasonic devices[a]	3 (1.5%)	0	3 (2.97%)	p = 0.246
Perfumes[a]	2 (1%)	1 (1.0%)	1 (1.0%)	p = 1.000

*p-values are considered exploratory.
[a] Measures in italics are considered to have no anti-vectorial prevention efficacy.

The "Knowledge, Attitude, Practices" (KAP) part of the study provided some relevant data. Only 3% of the subjects said they would never use repellents on their trip. This number is quite low compared to other surveys [30–32] and may be due to a bias as participants may have been zealous as they were seeking pre-travel health advice and were focused on applying repellents. Those seeking pre-travel advice have been shown to have a heightened awareness for mosquito borne infections and to be willing to use preventive measures [36]. The intention of a high proportion of travellers to use repellents may also be a result of the heightened media attention regarding the spread of mosquito-borne infections particularly the ZIKA virus. Some 146 (73.4%) of the subjects intended to use the repellents less often than every 5 h, i.e. the frequency of application that is usually recommended. This is an important finding especially in conjunction with the results showing

Table 6
Anti-vectorial prevention measures and number of travellers who intend to use them in travel destinations.

Measures	South America	South East Asia	East Africa	Southern Africa	West Africa	Central America	Middle East
Any measure	46 (71.8%)	46 (73.0%)	28 (100%)	14 (87.5%)	12 (92.3%)	7 (58.3%)	1 (33.3%)
Long sleeved clothing	36 (56.3%)	34 (54.0%)	23 (82.1%)	13 (81.3%)	8 (61.5%)	4 (333%)	1 (33.3%)
Mosquito net	26 (40.6%)	31 (49.2%)	20 (71.4%)	11 (68.8%)	6 (46.2%)	4 (33.3%)	1 (33.3%)
Light coloured clothing	9 (14.1%)	10 (15.9%)	8 (28.6%)	6 (37.5%)	5 (38.5%)	1 (8.3%)	–
Impregnation of clothes	11 (17.2%)	13 (20.6%)	4 (14.3%)	6 (37.5%)	2 (15.4%)	3 (25.0%)	–
Air conditioning	6 (9.38%)	9 (14.3%)	3 (10.7%)	1 (6.25%)	4 (30.1%)	2 (16.7%)	–
Perfumed candles[a]	*10 (15.6%)*	*3 (4.8%)*	-	*1 (6.25%)*	*3 (23.1%)*	-	-
Vitamin B[a]	*2 (3.1%)*	-	*1 (3.6%)*	-	*2 (15.4%)*	-	-
Ultrasonic devices[a]	*1 (1.6%)*	*2 (3.2%)*	-	-	-	-	-
Perfumes[a]	-	*1 (1.6%)*	-	-	*1 (7.7%)*	-	-

[a] Measures in italics are considered to have no anti-vectorial prevention efficacy.

that sub-optimal concentrations of repellents were applied. To compensate low application dosages, repellents could be applied more frequently and frequent application of low dosages may well provide reasonable repellent levels. However, it appears that travellers neither use adequate quantities of repellents nor do they apply them often enough. Sex and age have a major influence on the adherence to repellents. Women as well as the oldest age group applied higher doses of both repellents and also intended to use them more frequently. Young men applied the lowest doses. This will have an impact on the acquisition of vector-borne infections and may contribute, to some extent, to the male sex-bias for certain mosquito-borne infections such as malaria [37,38].

Regarding the other AVPM that the subjects intended to use beside repellents, travellers to Africa, the continent with the highest risk for malaria, showed the best adherence. More than 90% of travellers to Africa intended to use at least one further AVPM additionally to repellents (East Africa 100%, West Africa 92.3%, Southern Africa 87.5%). Travellers to South America (71.8%), South East Asia (73.0%) and Central America (58.3%) showed lower projected AVPM adherence rates. Comparing these results with previous studies, travellers to Africa showed better projected adherence rates, while the results of travellers to other destinations were similar [31,39]. Especially the number of travellers intending to use mosquito nets is highest in Africa (East Africa 82.1%, Southern Africa 81.3%, West Africa 61.5%), possibly because travellers to these regions might be more aware of malaria.

The most intended AVPM was wearing of long-sleeved clothing (59.5%). However, it is questionable whether travellers will really wear long-sleeved clothing permanently in hot temperatures. Only few travellers (12.5%) intended to use air conditioning and there was no difference between the travel destinations. Travellers may not be aware that air conditioning is one of the most effective AVPM. Furthermore, some travellers still intend to use measures like perfumed candles, vitamin B, ultrasonic devices, and perfumes, although they have been shown to be ineffective [40,41].

The strength of this study was the large number of subjects, 100 per repellent group, who provided reliable results for the applied amount of repellents. In our study, the circumstances were close to real life, but some further differences in application quantities may be expected when travellers are using repellents in areas with actual transmission of vector-borne infections. One weakness of the study is the fact that travellers were pre-selected, in that they were seeking pre-travel advice and we may thus have recruited, *per se*, more cautious, adherent individuals. The subjects were only interviewed before they were going on a trip and therefore they could only state which measures they intended to use and this may not reflect what actually will be used on the trip. However, more than half of the subjects had already travelled to regions endemic for mosquito borne infections and they did not intend significantly better adherence to AVPM than inexperienced travellers. The only exception was the impregnation of clothes, which seems to be better known among experienced travellers.

5. Conclusions

Even travellers who consciously seek out pre-travel advice and who are keen to use anti-mosquito measures do not apply adequate, protective quantities of repellent. Women and those aged over 40 years are the most likely adherent users of repellents and other AVPM. Most manufacturers give only sparse recommendations for the quantitative use of repellents, particularly on the repellent packaging, and many advise not to use them more than twice a day. It would be advantageous to improve these recommendations by suggesting an optimal dosage and frequency of application. Formulations containing only 20% or less active ingredient do not provide a sufficient protection against mosquito bites. Travellers going to areas endemic for mosquito borne infections should use repellents with at least 30% or more of active ingredient.

The pre-travel health advice consultation should provide more information on the application quantity and correct use of repellents, e.g. the skin should be completely wetted after application. Furthermore, pre-travel advice should also provide some information about possible adverse reactions after repellent application, such as a burning sensation on the skin, reddening of the skin, burning sensation in the airways, to allay fears of adverse events, which may decrease the adherence rates. Particular attention in the pre-travel advice consultation should be given to young male travellers, the group with the lowest adherence rates to AVPM.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2018.12.007.

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